

Amendments to the claims: the following listing of claims replaces all previous claim listings.

1 (currently amended). A process for the preparation of a recombinant polypeptide of interest, comprising

(i) fermentation of a prokaryotic host cell comprising a periplasm and being transformed with a recombinant expression system capable of bringing about secretion of a polypeptide of interest into the periplasm of said host cell, wherein said fermentation is performed in a fermentation medium under conditions such that the polypeptide of interest is secreted into the periplasm of the host cell, and

(ii) extraction of the polypeptide of interest from the periplasm by applying an osmotic shock to the host cells contained in the fermentation medium,

wherein said osmotic shock is performed by adding an agent directly to the fermentation medium.

2 (currently amended). The process according to claim 1, ~~wherein said osmotic shock is performed by adding an agent directly to the fermentation medium~~, wherein said agent is capable of creating after dilution with H₂O an osmotic pressure leading to disruption of the outer cell membrane of the host cell, and subsequent dilution with H₂O.

3 (original). The process according to claim 2, wherein the agent is selected from the group consisting of sucrose, sodium chloride, arginine, lysine, guanidine hydrochloride, Triton-X 100, polyethyleneimine, and suitable mixtures thereof.

4 (original). The process according to claim 3, wherein said agent is sucrose.

5 (original). The process according to claim 4, wherein the concentration of the sucrose in the fermentation medium when starting the dilution is about 20% weight/volume.

6 (original). The process according to claim 5, wherein the dilution factor of the sucrose-containing fermentation broth with H₂O is at least about 3 times.

7 (original). The process according to claim 1, wherein said prokaryotic host cell is a Gram-negative bacterium.

8 (original). The process according to claim 7, wherein said Gram-negative bacterium is selected from the group consisting of Escherichia coli, Pseudomonas sp., Enterobacter sp., Campylobacter sp. and Vitreoscilla sp.

9 (original). The process according to claim 7, wherein the Gram-negative bacterium is E. coli.

10 (original). The process according to claim 1, wherein the polypeptide of interest is selected from the group consisting of an interferon, an interleukin, a growth hormone, a growth factor, a cytokine, an enzyme, an enzyme inhibitor, an antibody and an antibody fragment.

11 (original). The process according to claim 1, wherein the polypeptide of interest is an interferon alpha 2.

12 (original). The process according to claim 11, wherein the interferon alpha 2 is selected from the group consisting of interferon alpha 2A and interferon alpha 2B.

13 (previously amended). A process for the preparation of a recombinant interferon alpha 2, comprising

(a) obtaining a crude preparation of a recombinant interferon alpha 2,

(b) applying the crude preparation to a multi-step chromatography comprising the following steps in sequence:

(i) cation exchange chromatography,

(ii) anion exchange chromatography,

(iii) hydrophobic interaction chromatography,

(iv) cation exchange chromatography, and

(v) size exclusion chromatography.

14 (previously amended). The process according to claim 13, wherein the crude preparation of the recombinant Interferon alpha 2 is obtained by a process comprising

(a) fermentation of a prokaryotic host cell comprising a periplasm and being transformed with a recombinant expression system capable of bringing about secretion of a recombinant interferon alpha 2 into the periplasm of said host cell, wherein said fermentation is performed in a fermentation medium under conditions such that the recombinant interferon alpha 2 is secreted into the periplasm, and

(b) extraction of the recombinant interferon alpha 2 from the periplasm by applying an osmotic shock to the host cells contained in the fermentation medium.

15 (original). The process according to claim 14, wherein said osmotic shock is performed by adding an agent directly to the fermentation medium, wherein said agent is capable of creating after dilution with H₂O an osmotic pressure leading to disruption of the outer cell membrane of the host cell, and subsequent dilution with water.

16 (original). The process according to claim 15, wherein the agent is selected from the group consisting of sucrose, sodium chloride, arginine, lysine, guanidine hydrochloride, Triton-X 100, polyethyleneimine and suitable mixtures thereof.

17 (original). The process according to claim 15, wherein said agent is sucrose.

18 (original). The process according to claim 17, wherein the concentration of the sucrose in the fermentation medium when starting the dilution is about 20% weight/volume.

19 (original). The process according to claim 18, wherein the dilution factor of the sucrose-containing fermentation broth with H₂O is at least about 3 times.

20 (currently amended). The process according to claim 13 24, wherein said prokaryotic host cell is a Gram-negative bacterium.

21 (original). The process according to claim 20, wherein said Gram-negative bacterium is selected from the group consisting of Escherichia coli, Pseudomonas sp., Enterobacter sp., Campylobacter sp. and Vitreoscilla sp.

22 (original). The process according to claim 20, wherein the Gram-negative bacterium is E. coli.

23 (original). The process according to claim 13, wherein said interferon alpha 2 is selected from the group consisting of interferon alpha 2A and interferon alpha 2B.

24 (new). The process according to claim 13, wherein said crude preparation is obtained from a prokaryotic host cell expressing said recombinant interferon alpha 2.